VETERINARSKI ARHIV 73 (6), 355-362, 2003

Experimental therapy of calf diarrhoea with ampicillin trihydrate

Elena Chaleva[1]*, and Yuliana Encheva[2]

[1]*Department of Veterinary Pharmacology and Toxicology, National Diagnostic Research Veterinary Institute "Prof. Dr. G. Pavlov", Sofia, Bulgaria*

[2]*Department of Physiology and Pathology of Newborn and Growing Animals, National Diagnostic Research Veterinary Institute "Prof. Dr. G. Pavlov", Sofia, Bulgaria*

CHALEVA, E., Y. ENCHEVA: Experimental therapy of calf diarrhoea with ampicillin trihydrate. Vet. arhiv 73, 355-362, 2003.

ABSTRACT

The efficacy of ampicillin trihydrate was evaluated in the treatment of 10 calves with profuse diarrhoea. Pathogenic serotypes of *Escherichia coli* were isolated in large number from faeces of calves with diarrhoea. Clinical, biochemical and bacteriological studies of calves with diarrhoea were carried out. Ampicillin trihydrate administered orally at a dose of 60 mg/kg body mass twice daily for 7 successive days was successful in all the calves treated.

Key words: diarrhoea, ampicillin, sodium, potassium, serum proteins, calves

Introduction

Ampicillin is a semisynthetic penicillin possessing bactericidal activity against both Gram-positive and Gram-negative organisms (ROLINSON and STEVENS, 1961).

It has been reported (JONES, 1964; FERRARI, 1974) to be effective against the following common species of animal pathogens: *Streptococcus* spp.,

* Contact address:
Assoc. Prof. Dr. Elena Chaleva, PhD., Department of Veterinary Pharmacology and Toxicology, National Diagnostic Research Veterinary Institute "Prof. Dr. G. Pavlov", 15 P. Slaveykov" Blvd. Sofia 1606, Bulgaria, Fax: +359 2 95253 06; E-mail: elena_chaleva@abv.bg

ISSN 0372-5480
Printed in Croatia

non-penicillinase-producing *Staphylococcus*, *Clostridium* spp., *Enterococcus* spp., *Pasteurella* spp., *Salmonella* spp., *Escherichia coli* and *Proteus* spp. Ampicillin, as an antibiotic, is of great practical value (CHALEVA, 1981; BROWN et al., 1991; TUFENKJI et al., 1991) because of its broad spectrum of action and high acid-stability allowing its per oral administration (DOYLE et al., 1961). Contrary to other acid-stable penicillins, the absorption of ampicillin-like antibiotics is quite uniformly and slightly affected by food intake (POOLE et al., 1968; BLACK, 1976). LARKIN (1972) reported on the distribution of orally administered ampicillin in young calves. Per oral administration of ampicillin trihydrate in calf colibacteriosis has been recommended by SHMIDOV and GHENSEROVSKAYA (1972) in a 24 h dose 90 mg/kg body mass for 3 days (3 times daily). Ampicillin trihydrate in a 24 h dose of 400-800 mg has been administered as tablets for 2-5 days to suckling calves suffering from enteritis, leading to the recovery of 90-96% of animals (NAKANE et al., 1975). Calves, 1 to 5 days old, are most often affected by colibacteriosis but in some cases - up to day 10 after calving (MOON, 1978). BRAGINSKAYA et al. (1969) have proved that ampicillin has a 4-times higher activity than benzylpenicillin and 2 times higher than tetracycline activity in 72 strains of *E. coli*, isolated from pathological materials.

The object of this work is to follow up the therapeutic effect of ampicillin trihydrate in calves with profuse diarrhoea, changes in total protein, protein fraction, ion exchange of sodium (Na^+) and potassium (K^+) in blood serum.

Materials and methods

Ampicillin trihydrate as gelatin capsules ("Balkanpharma - Razgrad" AD), equivalent to 100 mg ampicillin base was used. The studies were carried out on 10 calves of Bulgarian brown cattle breed with profuse diarrhoea: 5 males and 5 females, 2 to 10 days old and weighing 36-40 kg. The control group consisted of 5 clinically healthy calves (2 males and 3 females) of the same age. Microbiological studies of the faecal samples from the sick calves were carried out prior to and after treatment. More than 20 isolates were tested against a 10 μg disc of the antibiotic. Standard

methods were used to identify microorganism (HADJIDIMOVA, 1975). The animals were then clinically monitored for rectal temperature, food intake and general condition daily for 7 days. Calves from the experimental group were treated orally with ampicillin trihydrate at a dose of 60 mg/kg body mass, twice daily for 7 consecutive days. Calves with diarrhoea were fed 2 litres twice daily of a glucose and electrolyte mixture (DALTON, 1970) instead of milk, together with oral antibiotic ampicillin trihydrate.

Blood samples were obtained from the jugular vein using individual disposable syringes and needles. Blood samples were collected before treatment and on the 3rd and 7th days after administration of the initial dose. Serum was separated after centrifugation and stored at -20 ^{0}C until analyzed.

Total protein and protein fractions were measured by electrophoresis. Serum concentrations of sodium (Na^+) and potassium (K^+) were analyzed by flame photometry. The data were subjected to statistical analysis with Student's *t*-test.

Results

Faeces of the calves were normalized within the first three days, as a result of the ampicillin treatment. Elimination of pathological mucus in faeces was recorded up to the 3rd day. Enterotoxigenic *E. coli* was isolated from the diseased calves before treatment. The pathogenic microorganisms isolated in the same calves prior to treatment disappeared on day 3 and could not be established on day 7 after treatment. Clinical recovery also advanced rather early - between days 3 and 5. The affected calves showed a good tolerance to the drug, dosage and duration of treatment. Diarrhoeal syndrome was rapidly eliminated

The mean values of potassium and sodium ions in blood serum of the calf group treated twice daily with 2 litres of the glucose and electrolyte mixture, together with ampicillin trihydrate 2×60 mg/kg body mass for 7 consecutive days, are illustrated in Table 1.

The level of serum electrolytes in the sick calves - potassium and sodium were decreased at the beginning and then slowly restored during the process of recovering.

Table 1. Mean (± SD) serum Na^+ and K^+ concentrations in the control and experimental calves

	n	Control group	n	Calves with diarrhoea		
				Before treatment	3rd day	7th day
Na^+ (mmol/l)	5	143.5 ± 1.49***	10	120.5 ± 1.88	129.9 ± 2.04**	141.2 ± 2.42***
K^+ (mmol/l)	5	4.52 ± 0.10	10	3.97 ± 0.14	4.14 ± 0.16	4.37 ± 0.20

*** P< 0.001; ** P < 0.01

The following protein fractions were determined by the electrophoretic separation of blood serum of both experimental and control calves: albumin, á-globulin, â-globulin and ă-globulin (Table 2).

Their distribution showed obvious discrepancies prior to the treatment of calves compared to the control. Mean albumin values were about 31.29 ± 1.3 g/L in the control calves, whereas those values in the experimental animals prior to ampicillin trihydrate treatment were of the order of 24.0 ± 2.5 g/L. Later on an elevation was established on days 3 and 7 - up to 29.5 ± 1.5 g/L in the calves treated with the drug for 7 days. Changes in total protein quantity were observed simultaneously with fluctuations in protein fractions. As can be seen from Table 2, total protein quantity before treatment was reduced - 65.2 ± 4.3 g/L. On day 3 after the initiation of

Table 2. Serum proteins (g/L) concentrations in the control and experimental calves (mean ± SD)

Parameter	Control group	Calves with diarrhoea		
		Before treatment	3rd day	7th day
Total protein(g/L)	73.0 ± 5.0	65.02 ± 4.3	68.60 ± 5.5	73.5 ± 3.0
Albumin (g/L)	31.29 ± 1.3	24.0 ± 2.5	25.20 ± 3.2	29.5 ± 1.5
Globulin (g/L)	41.71 ± 1.67	41.20 ± 0.99	43.40 ± 1.13	46.22 ± 1.15**
α- globulin (g/L)	6.03 ± 0.54	5.20 ± 1.05	6.59 ± 0.50	7.28 ± 0.83
β- globulin (g/L)	15.19 ± 0.30	16.38 ± 0.30	14.56 ± 0.60	15.68 ± 1.06
γ- globulin (g/L)	20.49 ± 0.73	19.62 ± 1,12	22.25 ± 0.88	23.26 ± 1.06
A:G ratio	0.75 ± 0.04	0.60 ± 0.02	0.60 ± 0.05	0.70 ± 0.04

** P < 0.01

treatment, total protein level was still under the normal value, with a tendency to increase on day 7 - 73.5 ± 3.0 g/L. No lethal cases were observed in experimental and control animals. In all affected calves the clinical symptoms abated quickly and disappeared within the first several days after initiation of ampicillin treatment. Recurrences were not recorded.

Discussion

Results with regard to the values of sodium and potassium in blood serum were somewhat contradictory. TENNANT et al. (1972) established that sodium levels in both serum and plasma of sick calves were reduced, but other authors (BOYD et al., 1974) demonstrated that it was elevated. LEWIS and PHILLIPS (1974) showed that sodium concentration in plasma was reduced from 135 to 140 mmol/l in healthy calves, down to 125 - 130 mmol/l shortly before death. The two-times administration of ampicillin trihydrate, as gelatin capsules, in a dose of 60 mg/kg body mass for 7 days, very possibly enhanced the labiality of tissue-bound potassium ions, which probably determined the considerable increase of their serum concentration. That fact was associated with the reduced muscular tone of the affected animals observed by us. Sodium level in blood serum of the experimental group was decreased - about 23 mmol/l - as compared with the control group ($P<0.001$), but in the further stage of the disease it showed a tendency to increase (Table 1). Alterations in potassium level were less manifested. It appeared that those fluctuations in the level of potassium and sodium were associated with water metabolism and dehydration observed in some of the calves as the disease progressed. As a result of those changes in electrolytes in sick calves, dehydration advanced as well as disturbances in metabolism and loss of electrolytes, with a disorder in electrolyte balance (FISHER and McEWAN, 1967). Dehydration was mainly due to wastage of water and sodium from extra cellular fluids, from plasma in particular (LEWIS and PHILLIPS, 1973). It was established that 96 % of the loss in body mass was due to the water eliminated from the body (VENKOV, 1982). The loss of water referred mainly to extra cellular fluid.

The changes advancing in serum protein in the course if the disease, and afterwards, are of particular interest. It is significant that during the

period of diarrhoea, as well as afterwards, specific quantitative ratios were observed between albumin and globulin during the whole observation period. As a rule, the reduction of albumin quantity is accompanied by an increase in globulin quantity, although a relative reduction of globulin also developed throughout the stages of the disease. With comparison of the changes advancing in protein fraction of blood serum in the calves with profuse diarrhoea, it becomes obvious that the changes in albumin fraction, as well as those in globulin, are clearly manifested after ampicillin trihydrate treatment of the animals. The general increase of globulins on day 7 ($P<0.01$) is due to the increase of á-globulin and ă-globulin fractions. Therefore, it could be concluded that globulin fractions in that case compensated for the albumin loss to a certain extent (BARSANTI et al., 1977).

The results from studies on the therapeutic effects of ampicillin trihydrate in calf diarrhoea revealed that an oral dose of 60 mg/kg body mass for 7 successive days possesses a high therapeutic efficacy.

References

BARSANTI, J. A., F. KRISTENSEN, F. B. DRUMHELLER (1977): Analysis of serum proteins, using agarose electrophoresis in normal dogs and in dogs naturally infected with *Dirofilaria immitis*. Am. J. Vet. Res. 38, 1055-1058.

BLACK, W. D. (1976): Serum ampicillin levels in the calf: Influence of dosage, route of administration and dosage form. Can. J. Com. Med. Vet. Sci. 40, 341-345.

BOYD, J. W., J. R. BAKER, A. LEYLAND (1974): Neonatal diarrhea in calves. Vet. Rec. 95, 310-313.

BRAGINSKAYA, P. S., A. N. SHNEERSON, S. P. RESVAN (1969): Development of resistance to ampicillin in gram-negative organisms. Antibiotiki (in Russian) 14, 831-834.

BROWN, M. P., M. B. MAYO, P. R. GRONWALL (1991): Serum and synovial fluid concentrations of ampicillin trihydrate in calves with supportive arthritis. Cornell Vet. 81, 137-143.

CHALEVA, E. (1981): Concentration and retention time of ampicillin trihydrate in the blood serum at oral application to ruminant animals. Vet. Sci. (Bulgaria) 18, 78-84.

DALTON, R. G. (1970): The Husbandry and Diseases of Calves. (Loosmore, R. M. and Scott Inglis, J. S. Eds), pp. 77.

DOYLE, F. P., J. H. NAYLER, H. SMITH, E. R. STOVE (1961): Novel acidstable penicillins. Nature 191, 1091-1092.

FERRARI, A. (1974): L'ampicillina in terapia veterinaria. Clin. Vet. 97, 299-302.

FISHER, E. W., A. D. McEWAN (1967): Death in neonatal calf diarrhea. II The role of oxygen and potassium. Brit. Vet. J. 123, 4-7.

HADJIDIMOVA, D. (1975). Susceptibility test: agar dilution. In: Medical Diagnostic. Edit. Hadjidimova, D., Sofia, Medicina and Phiscul. pp. 498-506.

JONES, A. (1964): The activity of ampicillin and phenethicillin for bacteria isolated from veterinary sources. J. Com. Path. 74, 129-140.

LARKIN, P. J. (1972): The distribution of a 400 mg dose of ampicillin administered orally to calves. Vet. Rec. 90, 476-478.

LEWIS, L. D., R. W. PHILLIPS (1973): Experimental therapy of calf diarrhea with ampicillin trihydrate intracellular and extracellular ion concentration in neonatal calves. Ann. Rech. Vet. 4, 99-111.

MOON, H. W. (1978): Mechanisms in the pathogenesis on diarrhoeas. A review. J. Am. Vet. Med. Assoc. 172, 143-147.

NAKANE, Y., Y. NAKAYAWA, K. NASHIKATA, K. TERAUCHI (1975): Treatment of diarrhoea in calves with synthetic penicillin. J. Jap. Vet. Med. Assoc. 28, 623-627.

POOLE, J. W., G. OWEN, J. SILVERIO, J. M. FREYHOF, S. B. ROSENMAN (1968): Physicochemical factors influencing the absorption of the anhydrous and trihydrate forms of ampicillin. Curr. Ther. Res. 10, 292-303.

ROLINSON, G. N., S. STEVENS (1961): Microbiological studies on new broad-spectrum penicillin "Penbritin". Brit. Med. J. 2, 191-196.

SHMIDOV, P. N., V. K. GHENSEROVSKAYA (1972): Activity of ampicillin on colibacillosis in calves. Veterinaria (in Russian) 1, 45-50.

TENNANT, B., D. HARROLD, M. REINA-GUERRA (1972): Physiologic and metabolic factors in the pathogenesis of neonatal enteric infections in calves. J. Am. Vet. Med. Assoc. 161, 993-1007.

TUFENKJI, A. E., M. AVINERIE, G. LARRIEU, G. HOUIN, P. GALTIER (1991): Pharmacokinetics of ampicillin and pentobarbital in the course of subclinical fascioliasis in sheep. Res. Vet. Sci. 50, 75-80.

VENKOV, T. (1982): Acute diarrhea in newborn and young animals. In: Acute Diseases of Digestive and Respiratory Systems in Calves. (Venkov, T., Ed.), Sofia, Zemizdat, pp. 10-21.

Received: 23 July 2001
Accepted: 7 November 2003

CHALEVA, E., Y. ENCHEVA: Pokusna terapija proljeva teladi ampicilin trihidratom. Vet. arhiv 73, 355-362, 2003.

SAŽETAK

Učinkovitost ampicilin trihidrata bila je provjerena u liječenju 10 teladi s profuznim proljevom. Patogeni serovarovi bakterije *E. coli* bili su u velikom broju izdvojeni iz proljeva teladi. Provedene su kliničke, biokemijske i bakteriološke pretrage. Ampicilin trihidrat primijenjen peroralno u dnevnoj dozi 60 mg/kg tjelesne mase u tijeku sedam uzastopnih dana pokazao se djelotvornim u sve liječene teladi.

Ključne riječi: proljev, ampicilin, natrij, kalij, telad